AMENDMENTS

IN THE CLAIMS:

1. (Amended) A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting ~~mutant~~ hippocampal cells, with a presenilin gene mutation having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells to tetanic stimulation; and

determining the effect of said [agent] candidate drug on the synaptic potentiation of said mutant hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

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2. Please cancel Claim 2. [A method according to Claim 2, wherein said mutant cells are mutated in a presenilin gene.]

3. (Amended) [A] The method according to Claim 1, wherein [said mutant cells are] mouse hippocampal tissue slices comprise said mutant hippocampal cells.

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4. (Amended) [A] The method according to Claim 1, wherein said enhanced synaptic potentiation is a result of a change in the $GABA_A$ receptor pathway.

5. (Amended) A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mutant hippocampal cells, with a presenilin gene mutation having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to a tetanic stimulus;

measuring changes in potentiation with time of the mutant hippocampal cells and wild-type hippocampal cells and comparing the effect of said [agent] candidate drug on the synaptic potentiation of said mutant hippocampal cells as compared to the observed synaptic potentiation of said wild-type hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells as compared to the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

6. (Amended) A method for determining whether a mutation in hippocampal cells acts on a common pathway with a $GABA_A$ receptor antagonist, said method comprising [according to Claim 5, including the additional steps of]:

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contacting mutant hippocampal cells, with a presenilin gene mutation having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a $GABA_A$ receptor antagonist;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to tetanic stimulation; and

measuring changes in synaptic potentiation with time of [the] said mutant hippocampal cells and said wild-type hippocampal cells and comparing the effect of said $GABA_A$ receptor antagonist on said mutant hippocampal cells and said wild-type hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells without a "significant change" in the synaptic potentiation of the wild-type cells is indicative of the mutation acting on a common pathway with said $GABA_A$ receptor antagonist.

7. (Amended) [A] The method according to Claim 5, wherein said [agent] candidate drug is present with said wild-type hippocampal cells.

8. (Amended) A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mutant hippocampal cells, with a presenilin gene mutation having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to a tetanic stimulus at a first potential of glutamate currents and a second potential of $GABA_A$ currents;

measuring the synaptic response at each of the first and second potentials for [the] said mutant hippocampal cells and said wild-type hippocampal cells and comparing the effect of said [agent] candidate drug on said mutant hippocampal cells and said wild-type hippocampal cells; wherein a reduction in the enhanced synaptic response of the mutant hippocampal cells without a significant change in the synaptic response of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

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9. (Amended) A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mutant mouse hippocampal cells mutated in the presenilin-1 gene and having enhanced synaptic potentiation upon tetanic stimulation as compared to wild-type hippocampal cells, with a candidate drug;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to tetanic stimulation; and

comparing the effect of said [agent] candidate drug on said mutant hippocampal cells and said wild-type hippocampal cells upon tetanic stimulation;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells without a significant change in the synaptic potentiation of the wild-type cells is indicative of

activity of a candidate drug for the treatment of Alzheimer's disease.

10. (Amended) Slices of mouse hippocampal tissue containing cells having a mutation in a presenilin gene combined with a candidate drug that is not an antibody.

11. (Amended) Slices of mouse hippocampal tissue containing cells according to Claim 10, after tetanic stimulation.

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12. (Amended) Slices of mouse hippocampal tissue containing cells according to Claim 10, wherein said mutation is [the] a PS-1 Δ9 mutation.

Add new Claim 13.

bq 13. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting slices of mouse hippocampal tissue containing cells, having a PS-1 Δ9 mutation and having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells to tetanic stimulation; and

a3 determining the effect of said candidate drug on the synaptic potentiation of said mutant hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

REMARKS

The Claimed Invention:

The claimed invention is directed to methods for screening for drugs for the treatment of Alzheimer's disease, and to slices of mouse hippocampal tissue containing cells having a